

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: T. YOSHIMURA, et al.  
Application No.: 10/563,088  
Filed: DECEMBER 30, 2005  
For: PROCESS FOR PRODUCING 5-iodo-2-methylbenzoic acid  
Group AU: 1621  
Examiner: Lalitha Nagubandi  
Confirm. No.: 8126

**REQUEST FOR RECONSIDERATION****Mail Stop: AMEND – FEE**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

November 30, 2007

Sir:

In response to the Office Action dated July 31, 2007, the period for response having been extended for one (1) month by the attached Petition for Extension of Time, Applicants respectfully submit the following Remarks, traversing the rejection under 35 USC 103 set forth therein.

It is respectfully submitted that all of the presently pending claims patentably distinguish over the teachings of the references applied by the Examiner in rejecting claims in this Office Action dated July 31, 2007, that is, the teachings of U.S. Patent No. 5,892,138 to Singh, et al., Japanese Patent Document No. 2003-89673 (Aizawa, et al.), and Japanese Patent Document No. 2003-012597 (Igari, et al.), under the provisions of 35 USC 103.

It is respectfully submitted that the references as applied by the Examiner would have neither taught nor would have suggested such a process for producing 5-iodo-2-methylbenzoic acid as in the present claims, including wherein the reaction

step of iodinating-2-methylbenzoic acid is performed in the presence of a (1) microporous compound, (2) iodine, (3) an oxidizing agent and (4) acetic anhydride, and, in addition, wherein such method includes a purification step including one or more of sublimation, distillation and crystallization. See claim 1.

In addition, it is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such process as in the present claims, having features as discussed previously in connection with claim 1, and, additionally, wherein the microporous compound is  $\beta$ -form zeolite, as in claim 2, with further definition of the  $\beta$ -form zeolite as in claims 3-5; and/or wherein the oxidizing agent is iodic acid and/or periodic acid (see claim 6); and/or wherein the microporous compound is separated and recovered, followed by re-employment in the reaction step (see claim 7), with specified processing of the separated and recovered microporous compound as in claims 8-11; and/or wherein the reaction step is performed in acetic acid serving as a solvent (note claim 12); and/or wherein the purification step is crystallization (note claim 13), with further definition of the crystallization as in claims 14 and 15, and wherein after crystallization the solvent is removed from a mother liquor and a portion of a residue recycled in a crystallization system, as in claim 16.

Furthermore, it is respectfully submitted that the teachings of the applied references would have neither disclosed nor would have suggested such a high-purity 5-iodo-2-methylbenzoic acid produced by a process as in claims 1 and 7, including a specified maximum amount of specific materials as impurities (see claims 17 and 20).

In addition, and as will be discussed further infra, it is respectfully submitted that the evidence of record, that is, the evidence in the Examples and Comparative Examples in Applicants' specification, establish unexpectedly better results achieved by the present invention, wherein the reaction step of iodinating 2-methylbenzoic acid is performed in the presence of (1) a microporous compound, (2) iodine, (3) an oxidizing agent and (4) acetic anhydride, as compared with processes of the closest prior art and/or processes even closer than the closest prior art, and based thereon overcomes any possible prima facie case of obviousness established by the teachings of the applied references and clearly supports a conclusion of unobviousness of the present invention. In this regard, it is respectfully submitted that the experimental data in Applicants' specification must be considered in determining obviousness. See In re DeBlauwe, 222 USPQ 191 (CAFC 1984).

The present invention is directed to a process for producing 5-iodo-2-methylbenzoic acid, and to high-purity 5-iodo-2-methylbenzoic acid produced by such process.

As described on pages 1-5 of Applicants' specification, there have been known methods for synthesizing 5-iodo-2-methylbenzoic acid. However, these various known methods have problems. For example, various of the methods have a low yield and/or low selectivity and /or a low purity product, e.g., producing relatively large amounts of 3-iodo-2-methylbenzoic acid rather than 5-iodo-2-methylbenzoic acid. In addition, other methods utilize highly toxic materials, making such technique inappropriate for an industrial scale, or require complex processing, or require materials (e.g., sulfuric acid) which need burdensome treatment, and/or have high processing costs. It is desired to provide a high-efficiency industrial

process for producing 5-iodo-2-methylbenzoic acid through iodination of 2-methylbenzoic acid as starting material, which is a relatively simple production process and is able to product a high-purity product with high selectivity for the desired product, and provides the desired product at high yield.

Against this background, Applicants have found that iodination of 2-methylbenzoic acid serving as a starting material can be performed at high selectivity through iodinating 2-methylbenzoic acid in the presence of (1) a microporous compound, (2) iodine, (3) an oxidizing agent and (4) acetic anhydride, and that a high-purity product can be achieved at high yield and high efficiency by combining the reaction step with a purification step including sublimation, distillation and/or crystallization. Note the first full paragraph on page 6 of Applicants' specification. Note also the paragraph bridging pages 36 and 37 of Applicants' specification.

It is emphasized that the reaction in the presently claimed process is conducted in the presence of (1) a microporous compound, (2) iodine, (3) an oxidizing agent, and (4) acetic anhydride. It is respectfully submitted that the results of the present invention are achieved by using all of materials (1)-(4) as in the present claims, as seen in the Examples and Comparative Examples in Applicants' original disclosure.

Thus, attention is respectfully directed to Example 1 on pages 18 and 19 of Applicants' specification, together with Examples 2 and 3 on pages 19-21 thereof. Note also Comparative Example 1 on pages 21 and 22 of Applicants' specification, using a reaction mixture including sulfuric acid (compare with the process in Japanese Patent Document No. 2003-012597, wherein 2-methylbenzoic acid was reacted with iodine and periodic acid in the presence of sulfuric acid in AcOH). Note

also Comparative Example 2, also including sulfuric acid in the reaction mixture. Note that in Comparative Example 3, the procedure of Example 1 was repeated, except that iodic acid was not employed; and also note Comparative Example 4 on page 24, wherein the procedure of Example 1 was repeated, except that acetic anhydride was not employed. As can be appreciated from disclosures on pages 21-24 of Applicants' specification, unsatisfactory results were achieved in each of the Comparative Examples 1-4.

See also the other Examples and Comparative Examples in Applicants' specification; in this regard, note Comparative Example 5 on pages 31 and 32, which shows that when concentrated sulfuric acid was employed as an acid catalyst, purity and yield of 5-iodo-2-methylbenzoic acid were unsatisfactory; Comparative Example 6 on pages 32 and 33, disclosing that when sulfuric acid was employed as an acid catalyst, the formed 5-iodo-2-methylbenzoic acid crystals had a high iodine content, so that high-purity 5-iodo-2-methylbenzoic acid was not produced; and Comparative Example 7 on pages 33 and 34 of Applicants' specification, showing that when acetic anhydride was not employed, purity and yield of 5-iodo-2-methylbenzoic acid were unsatisfactory.

As can be seen from the foregoing, as well as from a full review of the Examples and Comparative Examples in Applicants' specification, it can be seen that by conducting the iodination reaction in the presence (1) the microporous compound, (2) iodine, (3) an oxidizing agent and (4) acetic anhydride, unexpectedly better results in selectivity and yield, as well as high purity, are achieved. It is respectfully submitted that the advantageous results achieved by the present invention would have been unexpected, and it is respectfully submitted that the

unexpectedly better results achieved according to the present invention support a conclusion of unobviousness thereof.

Igari, et al. discloses a method for producing monoiodo compounds of methylbenzoate, wherein such compounds are produced by directly iodizing methylbenzoate, a raw material, by using an iodizing agent together with an acid catalyst in a solvent. Specifically, this patent document discloses reacting 2-methylbenzoic acid with iodine and periodic acid in the presence of  $\text{H}_2\text{SO}_4$  in AcOH.

Aizawa discloses a method for separating and purifying an isomer mixture of iodo-2-methylbenzoic acid, the method changing the iodo-2-methylbenzoic acid mixture comprising 3-iodo-2-methylbenzoic acid and 5-iodo-2-methylbenzoic acid to corresponding metal salts, adjusting the pH of the aqueous solution of the metal salts to  $5.0 \pm 0.5$  at normal temperatures, and separating precipitating crystals as 5-iodo-2-methylbenzoic acid as a principal compound by filtration, and separating the 3-iodo-2-methylbenzoic acid as a principal compound by adjusting the pH of the filtrate to 3.0-2.0 by addition of an acid. Note the English abstract of Aizawa, et al.

It is respectfully submitted that neither of Igari, et al. or Aizawa, et al., either alone or in combination, would have disclosed or would have suggested such a process as in the present claims, including the reaction being conducted in the presence of all of (1) a microporous compound, (2) iodine, (3) an oxidizing agent and (4) acetic anhydride, and advantages achieved due thereto.

It is respectfully submitted that the additional teachings of Singh, et al., even in light of the combined teachings of Igari, et al. and Aizawa, et al., would not have rectified the deficiencies of the teachings of Aizawa, et al. and Igari, et al., such that

the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art.

Singh, et al. discloses a process for the preparation of halocumenes. The process includes reacting cumene with a halogenating agent in a liquid phase in the presence of an aliphatic carboxylic acid and a specified microporous zeolite catalyst. Note column 2, lines 19-32. See also column 2, lines 49-56.

Initially, it is respectfully submitted that the teachings of Singh, et al. would not have been properly combinable with the teachings of the two applied Japanese patent documents. Thus, each of the two applied Japanese patent documents are directed to providing iodo compounds of methylbenzoic acid or ester thereof. In contrast, Singh, et al. is directed to preparation of 4-halocumenes. In view of different technologies involved in the two Japanese patent documents, on the one hand, and in Singh, et al., on the other, and in view of different problems addressed by each, it is respectfully submitted that one of ordinary skill in the art concerned with in the two Japanese patent documents would not have looked to the teachings of Singh, et al.

Furthermore, in view of the different technologies, as well different problems addressed by the applied references, as discussed previously, it is respectfully submitted that there would have been no reason to combine the teachings of the applied references, as combined by the Examiner, absent hindsight use of Applicants' disclosure, which of course is improper under the requirements of 35 USC 103.

In any event, even assuming, arguendo, that the teachings of the three references applied by the Examiner were properly combinable, such combined

teachings would have neither disclosed nor would have suggested the presently claimed process, including wherein the reaction takes place in the presence of all of a microporous compound, iodine, an oxidizing agent and acetic anhydride.

It is respectfully submitted that the Examiner has not established a prima facie case of obviousness, even assuming, arguendo, that the teachings of the applied references were properly combinable. Thus, note that on page 4 of the Office Action dated July 31, 2007, the Examiner indicates that a difference between the present method and Aizawa, et al. "is that the instant process requires a microporous compound for the iodination to be carried out in presence of acetic anhydride", and the Examiner goes on to discuss the microporous compound. It is respectfully submitted, however, that the Examiner has not even alleged, much less established, that the combined teachings of the references would have disclosed or suggested the reaction taking place in the presence of, inter alia, the acetic anhydride. It is respectfully submitted that the Examiner has not established that the combined teachings of the applied references would have disclosed or would have suggested the presently claimed process, wherein the reaction is carried out in the presence of the materials as in the present claims, much less advantages thereof, or wherein the recited purification step is also conducted, as in the present claims.

In addition, it is respectfully submitted that the Examiner errs in conclusions concerning yield and purity within the teachings of the applied prior art. Specifically, Applicants respectfully traverse the conclusion by the Examiner that the process of Igari, et al. yields 95.7% of 5-iodo-2-methylbenzoic acid. That is, it is respectfully submitted that Igari, et al. teaches that the process thereof yields 52-70% of 5-iodo-2-methylbenzoic acid, with purity of 5-iodo-2-methylbenzoic acid being 95.7%. Note



the abstract of Aizawa, et al. shows a 54% reaction product mixture. Clearly, the yield in Igari, et al. is much less than 95.7% of 5-iodo-2-methylbenzoic acid, as alleged by the Examiner.

The Examiner points to Singh, et al. as disclosing halogenation in the presence of microporous compounds like zeolites. However, even were zeolites to be utilized in the process of either and/or both of the applied Japanese patent documents, such combination would not have disclosed or would have suggested the present invention, or achieved advantages achieved by the present invention. Thus, in this regard, attention is respectfully directed to Comparative Example 4 of the above-identified application, on page 24 of Applicants' specification. In Comparative Example 4, the procedure of Example 1 was repeated, including, e.g., a specified form of zeolite, but in Comparative Example 4 no acetic anhydride was employed. As stated on page 24 of Applicants' specification, when acetic anhydride is not employed, purity and yield of 5-iodo-2-methylbenzoic acid were unsatisfactory. Thus, even assuming, arguendo, that the teachings of the references as applied by the Examiner were combined, such teachings would have neither disclosed nor would have suggested the presently claimed process, including wherein the reaction was performed in the presence of all of the materials as recited in all of the present claims, and advantages achieved due thereto.

Furthermore, attention is respectfully directed to the high purity product as in various of the present claims, having a purity of at least 99%, and which contains specified impurities in very small amounts. It is respectfully submitted that the combined teachings of the applied references do not disclose, nor would have suggested, the high purity product, and advantages due thereto.

In view of the foregoing comments, reconsideration and allowance of all claims presently pending in the above-identified application are respectfully requested.

To the extent necessary, Applicants hereby petition for an extension of time under 37 CFR 1.136. Kindly charge any shortage of fees due in connection with the filing of this paper, including any extension of time fees, to the Deposit Account of Antonelli, Terry, Stout & Kraus, LLP, Account No. 01-2135 (case 396.45629X00), and please credit any overpayments to such Deposit Account.

Respectfully submitted,

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